The Center for Research on Environmental Disease

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2008

In this issue...

Message from the Director

Greetings! Since our last newsletter Center activites continue to move forward at a fast pace. We have hosted our External Science Advisory Board (ESAB), attended the NIEHS Core Center Directors Meeting, and held a successful annual retreat. First, we were visited by our ESAB on September 23rd. Members present were Drs. Gerald Wogan (Chair), David Christiani, Shuk-mei Ho, Serrine Lau, Leona Samson, Gary Stoner, Steve Safe, Henry Thompson and Paul Meltzer. As always, the ESAB was extremely helpful and we appreciate their valuable input on our current activities and future plans for the Center.

The Annual CRED Retreat was held October 23rd & 24th, at the Festival Institute in Round Top, Texas. This years retreat focused heavily on science and included a Keynote address from Dr. Christopher Austin, Director of the NIH Chemical Genomics Center, and Senior Advisor for Translational Research at NHGRI. In an effort to maximize scientific interactions, CRED members were encouraged to sponsor an individual from his or her laboratory to present a poster at the meeting on Thursday night. The retreat was a wonderful opportunity for the Ph.D. students and post-docs who attended to get some individual attention for their projects, and to interact with faculty from across the Center. Turn to pages 3 & 4 in this issue for more on the retreat. It is events like these, and the communication that arises from them, that help make our Center so successful.

Finally, in this issue Dr. Andrea Gore provides a topical article on Endocrine Disruption and the COEC provides updates on their recent activities. Also, those interested in submitting innovative proposals for the 2009 Pilot Project Program will find more information on page 9.

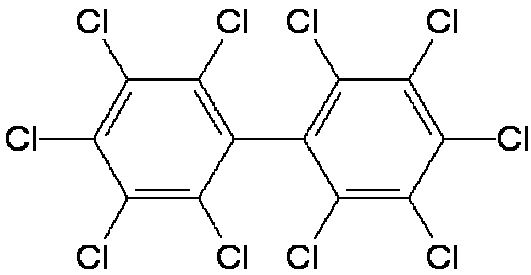
Sincerely,

Endocrine Disruption

Andrea C. Gore, Ph.D.
Professor, Pharmacology & Toxicology
Member, Research Focus Area 4, Genetics and Epigenetics of Early Life Exposures

The struggle of young couples with infertility is not just a perception: the United Nations Population Division reported that the average fertility rate for women, an index of fertility adjusted for age, has declined from 3.45 in 1955 to 2.04 in 2005. Epidemiological research in men shows that sperm count has declined 50% during the past fifty years. The incidence of reproductive tract abnormalities in newborn infants, including undescended testes (cryptorchidism), underdeveloped urinary tracts and penile malformations (hypospadias), and ambiguous genitalia are also on the rise.

These declines in human fertility over the second half of the 20th century were coincident with losses of animal populations due to aberrant reproductive behaviors or traits. The near extinction of American bald eagles; the occurrence of alligators with penises so small that they were unable to mate; fish whose gonads were a mixture of both ovarian and testicular tissue types (intersex); and drastic declines in populations of Arctic mammals such as polar bears and seals, were being reported. Scientists began to suspect that a major culprit contributing to these phenomena was increased contamination by industrial chemicals and pesticides. For example, lubricants for heavy machinery (PCBs), powerful pesticides (DDT) and other chemicals came into widespread usage after World War II. In some cases, these chemicals were not stored carefully, and they leaked into the soil or water systems. In addition, the highly toxic compound dioxin was often produced as a side product in the synthesis of organochlorine chemicals. Studies evaluating levels of these compounds in wildlife showed a direct correlation between those animals with the highest body burden of contaminants and a failure to reproduce successfully.

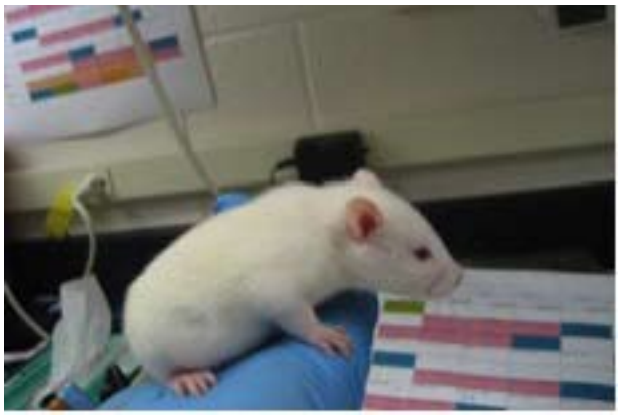


Chemical structure of a representative PCB.

These links between environmental contamination and compromised reproductive function launched the field of endocrine disruption. An endocrine-disrupting compound (EDC) is a substance that interferes with normal endocrine processes and has deleterious effects on reproduction and endocrine physiology. The classes of compounds that scientists consider EDCs are very broad, and they include not just PCBs, dioxins and pesticides, but also some heavy metals, fungicides, flame retardants, plasticizers and even some pharmaceuticals.

In the past twenty years, laboratory scientists have provided important experimental evidence showing that EDCs diminish reproductive success, and in addition, they have begun to identify the mechanisms by which this happens. Two very important points have emerged in understanding how endocrine disruptors work. One key is the link between EDCs and natural hormones, especially estrogens, which are produced in all female and male vertebrates. The second key to endocrine disruption is the timing of exposure. During early development, male fetuses actually have higher levels of estrogens than do females. These normal sex differences in estrogens (high in males, low in females), if perturbed, result in aberrant sexual development. Thus, fetal exposures to EDCs that activate or block estrogen receptors, depending upon the compound, may result in permanently compromised fertility in adulthood in a sex- and developmental stage-dependent manner. Both of these points were illuminated in humans by the example of DES (diethylstilbestrol), an estrogenic pharmaceutical that was prescribed to millions of pregnant women to prevent miscarriage. It was discovered that the fetuses exposed to this exogenous estrogen during key developmental periods had a significantly increased incidence of reproductive tract abnormalities and cancers later in life.

The case of DES launched the scientific discipline known as the “fetal basis of adult disease” and provided the basis for work undertaken in my laboratory at The University of Texas at Austin and the Center for Research on Environmental Disease (CRED). We are seeking to understand the specific mechanisms for how environmental EDCs given during the embryonic developmental period perturb reproduction in adulthood. Two members of my laboratory group, Dr. Rebecca Steinberg



Fetal treatment of rats with low-levels of PCBs does not cause any obvious deformities, but results in rats that have aberrations in reproductive function.

(now a postdoctoral fellow at UT-Austin) and Sarah Dickerson, a current Pharmacology and Toxicology graduate student, have led this project. We are using PCBs as our model, and administering very low levels to pregnant rats at a dosage that is estimated to be very similar to environmental PCB exposure in pregnant women. In our rats, following low-dose fetal exposures, the pups appear externally to be normal and healthy. As they mature, however, we have noted that they have compromised reproductive physiology and behaviors. We also allowed these animals to give birth to produce a "grandchild" generation, and the grandchildren exhibited dysfunctions in their hormone levels. Because we are interested in the role of the estrogen receptors that may mediate the effects of PCBs, we have evaluated the expression of estrogen receptors in the brains of the exposed adults. We found substantial changes in numbers and distribution of these receptors in the PCB compared to the control (vehicle) counterparts. These data suggest that low levels of EDC exposure during a key fetal developmental period causes subtle aberrations in reproductive function, and that the mechanism may involve actions of PCBs on the estrogen receptors during a critical life stage.

2008 CRED Retreat Update!!

The Center retreat was held in Round Top, Texas on October 23 & 24 at the International Institute - Festival Hill. We were extremely pleased with a turnout of 52 participants from Science Park-Research Division, UT Austin, MDACC and UTHSC - SPH. Both days included informative presentations by Center Members highlighting current work across all four Research Focus Areas (RFAs). Day 1 included a Keynote address by Dr. Christopher P. Austin, who is Director of the NIH Chemical Genomics Center, and Senior Advisor for Translational Research at NHGRI. Followed by dinner, a scientific poster session, and a social gathering, accompanied by live entertainment where plenty of stimulating discussions and opportunities to explore possibilities for collaboration lasted into the evening. Day 2 continued with RFA research highlights, and a workshop after lunch on "Small Molecule Screening Approaches in Drug Development and Biological Research" co-moderated by Drs. Mark Bedford, Christopher Austin, and Michael Mancini (Baylor College of Medicine). Finally, a poster session was held with representatives from each Facility Core providing individual consultations at the closing reception. You may view a synopsis of the agenda along with additional pictures on the following page.

Presentations were held in the Edyth Bates Old Chapel at The International Festival Institute at Round Top.

Photos are courtesy of Dr. John Richburg, CRED Associate Director.

Dr. John DiGiovanni, Director, welcomes CRED Members.

2008 CRED Retreat Agenda

KEYNOTE ADDRESS

Discovery of Chemical Probes of Biology and Development of New Therapeutics

Christopher P. Austin, M.D., Director, Chemical Genomics Center, and Senior Advisor for Translational Research, National Human Genome Research Institute, NIH

WORKSHOP

Small Molecule Screening Approaches in Drug Development and Biological Research

Mark Bedford, Ph.D. (MD Anderson Cancer Center, SPRD), Moderator; Michael Mancini, Ph.D. (Baylor College of Medicine) and Christopher Austin, M.D. (NIH) Co-Moderators

SPEAKERS:

Modeling the Human p53 R72P Polymorphism in Mice -
David Johnson, Ph.D., M. D. Anderson Cancer Center, SPRD

Exposure and Risk Disparities between Mexican-American and non-Hispanic White Populations in Houston -
Diana Hun, University of Texas at Austin

Genome-wide Association Studies in Lung Cancer: Hunting the Snark on Chromosome 15 (far from the jubjubs and bandersnatch) -
Chris Amos, Ph.D., M. D. Anderson Cancer Center, Houston

Genetic and Environmental Risk of Glioma -
Melissa Bondy, Ph.D., M. D. Anderson Cancer Center, Houston

Transgenerational Effects of Endocrine Disruptors -
Andrea Gore, Ph.D., University of Texas at Austin

Dietary Energy Balance Impacts Pancreatic Lesions in the K5.COX-2 Transgenic Model of Pancreatic Cancer -
Lauri Lashinger, Ph.D., University of Texas at Austin

Alcohol Consumption Promotes Breast Cancer Progression by Sensitization to Hormones -
Nomeli Nunez, Ph.D., University of Texas at Austin

Energizing the Warburg Effect and Prevention of Skin Carcinogenesis with Uncoupled Mitochondrial Respiration -
Cory Ungles, University of Texas at Austin

Obesity and Diabetes in Association with Risk and Survival of Pancreatic Cancer -
Donghui Li, Ph.D., M. D. Anderson Cancer Center, Houston

Evaluation of Novel Markers of Susceptibility to Tobacco Carcinogens
Randa El-Zein, Ph.D., M. D. Anderson Cancer Center, Houston

Regulation of Histone Methyltransferases by Estrogen Receptor Signaling: A Mechanism for Xenoestrogen-Induced Developmental Reprogramming
Tiffany Bredfeldt, Ph.D., M. D. Anderson Cancer Center, SPRD

DNA Methylation Causes Genetic Instability by Altering DNA and Chromatin Structures
Karen Vasquez, Ph.D., M. D. Anderson Cancer Center, SPRD

Live music accompanied scientific interactions at Thursday nights poster session. *Pictured left to right are Drs. Rick Wood (RFA2), John DiGiovanni (CRED Director) and Fernando Benavides.*

The retreat provided a great opportunity to view scientific posters and participate in discussions about research interests, future goals and possible collaborations.

STEER

Short Term Educational Experiences for Research

In 2007 the CRED COEP received a highly competitive NIEHS STEER (Short Term Research Educational Experiences for Research) to support the continuation and expansion of the EHS Summer Undergraduate Research Program (EHS-SURP). Associated with the program for the undergraduates are the EHS High School Research Program (EHS-HSRP) and the Public Health Student Internship. The overall goal of EHS-SURP/EHS-HSRP is to provide an authentic, hands-on, academic or summer research experience for talented undergraduate/high school students with the objective of promoting careers in environmental science and health research. The goal of the Public Health Internship is to provide practicum experience and extend studies into the arena of public health research and policy. The 2009 EHS-SURP will be held June 8, 2009 through August 14, 2009. Undergraduate students who are interested in applying online can visit our website at http://cred.mdanderson.org/surp and high school students should contact Erin Herbrich for further details at eherbric@mdanderson.org.

The 2008 Summer Students

Row 1: Kelly Huang, Ran Lie, Kelsey Zimmermann, Lindsey Wiggins, Xi Chen

Row 2: Erin Herbrich (COEP Staff Member), Simran Madan, Emily CVer Hoecve, ,Sitara Paladuhu, Praveena Paladugu, John Valenta, Jennifer Razek, Frances Cervoni, Jezziel Barrera

Row 3: Kimberly Ngo, Mari Allison, Bojan Jokic, Benjamin Crysup, Ross Gillette, James Howard, Michael Bernauer, Stephen Meyer

Scientist Presents New Spin on Periodic Table Lesson

The "Scientists in the Schools" program is a component of the CENTIPEDe (Community Education Networks to Integrate Prevention of Environmental Disease) Project supported by a HHMI Precollege Education Program grant. On September 30th and October 1st, 2008, CRED faculty member and COEC Associate Director Dr. David Mitchell provided a short lecture and conducted hands-on activities to teach 8th graders about the periodic table of elements. Dr. Mitchell discussed the history of the periodic table and engaged the students with hands on activities and technology. In one activity, students "became" the elements and formed various chemical compounds and investigated their properties. Another activity designed to illustrate atomic weight involved comparing the properties of a lead brick versus a block of wood of the same dimensions. During the program, students also viewed the YouTube "Periodic Table of Rock" music video, and teachers reported that the students were singing the song weeks after the program.

The students brought the periodic table to life as they "became" the elements and formed various chemical compounds.

Dr. Mitchell discusses with students the difference in atomic mass between a lead brick and a block of wood.

Community Science Night (CSN) Live

Mistress of ceremonies, Dr. Irma Gimenez-Conti

Another component of the CENTIPEDe Project is the Community Science Night Live (CSN Live). The goal of CSN is to enhance scientific literacy, encourage community support of K-12 science education and to increase public understanding of current research discoveries. The first CSN was held May 22nd 2008 at the Smithville Recreation Center. More than 130 residents of the Smithville community attended and listened to environmental health promotion talks by CRED Faculty and viewed scientific demonstrations and poster presentations by SISD students. Speakers included Dr. David Mitchell, who discussed "Sunlight and Skin Cancer Risk" and Dr. Steve Hursting, who talked about "Diet, Obesity and Cancer Risk." Dr. Irma Gimenez-Conti served as the mistress of ceremonies.

The next CSN Live will be held in conjunction with The Smithville Festival of Lights on Saturday, December 6th, 2008 from 10 am - 5 pm. The COEP will have a booth where students, parents and all community members can discuss research activities and environmental health issues with SPRD scientists and staff. The booth will also feature an array of Smithville student science projects, scientific displays, games and brochures with environmental disease and cancer prevention information. If you are interested in participating in this event, please contact Heather Reddick at hreddick@mdanderson.org.

Students display their science projects at the first CSN Live.

CRED COEC staff members Joe Rodriguez and Mary Henderson prepare fliers and supplies for transport to Houston

On the morning of September 13, 2008, Hurricane Ike, the third most destructive hurricane to ever hit the United States, approached the Texas coast near Galveston Bay, making landfall over the east end of Galveston Island. In the aftermath of the storm, the CRED COEC in collaboration with members of the NIEHS Center in Environmental Toxicology at the University of Texas Medical Branch at Galveston (UTMB), Texas Environmental Justice Advocacy Services (TEJAS), and the Louisiana Action League (LAL) launched an effort to provide needed cleaning supplies and safety and clean up information to those on Galveston Island. The CRED COEC printed approximately 6,000 fliers (3 in English, 3 in Spanish) explaining safety precautions for 1) entering your house after a hurricane or flood, 2) mold and germ remediation and, 3) lead remediation.

While COEC personnel were able to find Spanish language fliers from the Centers for Disease Control and Prevention (CDC) website on mold and germ cleanup with bleach, there were no translated materials on the important issues of home re-entry or lead remediation. Dr. Irma Gimenez-Conti, Associate Director of the COEC and Carlos Quintanilla, of the Histology Core, translated fliers from the HealthyVoices.org website into Spanish. These materials were originally developed by the NIEHS Center at the University of New Mexico, in response to similar informational needs following hurricane Katrina.

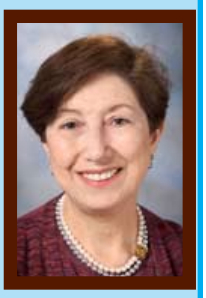
The employees of SPRD generously donated desperately needed supplies such as: mosquito repellent, large heavy trash bags, flashlights and batteries, bottled water, bleach, mops, etc., and the CRED COEC supplemented the supplies through a trip to Wal-Mart. The fliers and supplies were transported, by Joe Rodriguez of the CRED COEC, to Houston to join with other donations, including protective masks from the Gulf Coast Society of Engineers and re-entry kits from the LAL. Juan Parras of TEJAS coordinated the consolidation of the supplies and fliers and delivery. Mr. Parras became emotional when he saw all the supplies that had been donated by SPRD personnel and reported that it was the single biggest donation from any organization. Our friends at UTMB Galveston reported that the items went “like hotcakes” through the Red Cross distribution PODS. The fliers were also posted on the UTMB website and distributed by federal emergency teams manning the UTMB emergency department. The COEC sincerely appreciates all of the generous contributions from SPRD personnel.

Left: Just some of the many generous donations from the people of Science Park - Research Division.

Right: A staff member at TEJAS displays fliers that were provided by the CRED COEC.

News about us...

Robert M. Chamberlain, Ph.D. became Chair, Ad Interim, of the Department of Epidemiology on September 1, upon the retirement of Margaret R. Spitz, M.D., MPH. Dr. Spitz will continue directing her research projects on lung cancer in a part-time capacity at MDACC, following her retirement.



Welcome New Member...

Richard D. Wood, Ph.D., was appointed as a full member to Research Focus Area 2, Mechanisms of Environmental Carcinogenesis. Dr. Wood's research interests focus on DNA repair mechanisms and damage responses, DNA polymerases, DNA damage tolerance, genetic dependence of mutagenesis and carcinogenesis.

Congratulations to...

Maria Hernandez-Valero, Dr.P.H., Instructor in the Department of Health Disparities Research was recently awarded a Fulbright Scholarship, and will be going to Mexico to study phthalate exposure in women with breast cancer. Congratulations to Dr. Hernandez-Valero on this prestigious honor.

Xifeng Wu, M.D., Ph.D., Professor of Epidemiology in the Division of Cancer Prevention and Populations Sciences, is the recipient of both the Julie and Ben Rogers Award for Excellence in Research and the UTMDACC Faculty Achievement Award for 2008. We congratulate Dr. Wu on these prestigious awards.

CRED Members *in the News*

Titles below link to full press releases.

Creating Lung Cancer Risk Models For Specific Populations Refines Prediction

Lung cancer risk prediction models are enhanced by taking into account risk factors by race and by measuring DNA repair capacity, according to some CRED members of the Department of Epidemiology in two corresponding papers that appeared in the September issue of Cancer Prevention Research.

Protein "Switch" Suppresses Skin Cancer Development

Drs. DiGiovanni and Fisher are among a group of researchers in the Department of Carcinogenesis at Science Park-Research Division and reported in the September 9 issue of Cancer Cell that the protein IKKalpha (IKKa) regulates the cell cycle of keratinocytes and plays a key role in keeping these specialized skin cells from becoming malignant.

Gene Variations Alter Risk of Esophageal Cancer

Dr. Xifeng Wu, is actively involved in a study, which is the first to look at the association between variations in genes related to microRNAs and esophageal cancer. Results of the study show variations in a common gene pathway may affect esophageal cancer risk.

CRED ANNOUNCEMENTS....

✓ Publications

Please remember to acknowledge the Center grant number P30 ES007784 on any papers that have relevance to Center goals or that take advantage of Center Facility Cores. If you have any questions regarding Center activities or your Center status, please do not hesitate to contact the CRED Administrative Office at (512) 237-9444. To read more visit **NIEHS Acknowledgement**.

✓ Progress Report

The Annual Progress Report is due February 1. The CRED office will be contacting various members in the very near future for updates and information needed to complete the continuation progress report.

✓ 2009 Pilot Project Program

Send us your Pilot Project Program Pre-Proposals for 2009!
For more details & forms, please visit our website:
http://cred.mdanderson.org
Pre-Proposals are due January 16, 2009

PROGRAM OVERVIEW

The CRED is currently accepting applications for the Thirteenth Annual Pilot Project Program, to be funded in 2009. Successful applications will target important areas of research in the field of Environmental Health Sciences that relate directly to the mission and goals of the CRED.

The overall objective of the CRED is to study the mechanisms by which environmental factors may cause or influence human disease and to develop methods for early detection, prevention, and control of environmentally related diseases. The theme is to define host responses to environmental exposures and to understand how diet and genetic background influence these responses. Topics of interest to the CRED range from basic mechanisms of toxicity in model systems, through mechanisms by which environmental stimuli cause disease, to population-based studies that relate exposures, dietary factors or genetic factors to human diseases (including cancer).

Two types of Pilot Projects will be eligible for funding this round. Basic research proposals that conform to Center objectives and the Center theme will be considered with budgets up to $30,000. In addition, we wish to fund research designed to facilitate the translation of basic findings to the clinical or public health setting. The second type of Pilot Project will require extensive collaboration between basic researchers and population-based researchers, facilitated by our newly established Integrative Health Sciences Facility Core (FC5). In addition to the basic funding level of $30,000 supplemental funding up to $20,000 per year will be available for these population-based studies, which may require extensive sample recruitment and/or sample collection costs. For both types of Pilot Project, awardees who are not Center Members will also be given access to the Center's Facility Cores, and allotments to help cover the costs of services in the Cores.

Upcoming Seminars....

2008

November 20, 2008
Pengbo Zhou, Ph.D.
Associate Professor
Weill Cornell Medical College, New York
Host: Dr. Dean Tang, UTMDACC-SPRD
Ubiquitin, Nucleotide Excision Repair, and Skin Cancer

December 16, 2008
Tanya Paull, Ph.D.
University of Texas at Austin
Host: Dr. David Johnson, UTMDACC-SPRD
DNA End Processing by Mre11/Rad50 Complexes

2009

January 20, 2009
Dan Yarosh, Ph.D.
AGI Dermatics
Host: Dr. Rodney Nairn, UTMDACC-SPRD
The Intercellular Communication of DNA Damage and its Repair

January 22, 2009
Gail Prins, Ph.D.
University of Illinois at Chicago
Host: Dr. Robin Fuchs-Young UTMDACC-SPRD

February 17, 2009
Marilyn Diaz, Ph.D.
NIEHS
Host: Dr. Rodney Nairn, UTMDACC-SPRD
Rev3-mediated Mutagenesis in Mamalian cells

March 4, 2009
Casey Wright, Ph.D.
University of Texas at Austin
Host: Dr. David Johnson, UTMDACC-SPRD
Regulation of NF-kappaB signaling in lymphoma

March 17, 2009
Tom Misteli, Ph.D.
NCI
Host: Dr. Rodney Nairn, UTMDACC-SPRD
Spatial Genome Organization in the Formation of Translocations and DNA Repair

April 30, 2009
Steven Kliewer, Ph.D.
University of Texas - Southwestern Medical Center
Host: Dr. Cheryl Walker, UTMDACC-SPRD
Nuclear Receptors and FGFs in Metabolism: From Feast to Famine

Seminars are received or sent to other Campuses via videoconference. Contact the CRED office for information.

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***If you would like to be added to our mailing list**, please contact Sydni McGahan in the CRED Administrative Office at 512/237-9444 or e-mail smcgahan@mdanderson.org*
Visit our website at http://www.cred.mdanderson.org

***This newsletter is made possible by** grant P30 ES007784 from the National Institute of Environmental Health Sciences, NIH, and is published by the Center for Research on Environmental Disease, a joint NIEHS funded Center between The University of Texas M. D. Anderson Cancer Center, Science Park-Research Division and The University of Texas at Austin.*

NIEHS Center Program
The University of Texas School of Public Health
The University of Texas at Austin
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